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Early diagnosis of severe congenital malformations by ultrasonography

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1 Introduction

Ultrasonographic examination was introduced for the most common fetal neural-tube defects such as anencephaly, spina bifida etc. by CAMPBELL et al. [6, 8]. In 1972, CAMPBELL et al. [6] recommended ultrasound examination as a screening method for anencephalic fetuses. Besides ultrasonographic investigation, determination of alpha-fetoprotein values from amniotic fluid is a standardized test for the exclusion of neural tube defects [3] in selected populations. HOBBINS et al. [16] and KRATOCHWIL [19] have emphasized the leading role of ultrasound in the detection of congenital anomalies. A review of sonographically detectable malformation syndromes has been presented by KURJAK [20, 21]. **With the aid of modern ultrasound equipment (real-time scanning with high resolution and grey-scale storage), it has become much easier and less time consuming to detect severe malformation syndromes in the first half of pregnancy.** This paper presents five examples of fetal malformations. In four of them, diagnosis was performed in the first trimester and one diagnosis was made at the beginning of the second trimester of pregnancy (see Tab. I).

2 Methods

2.1 Ultrasound examinations

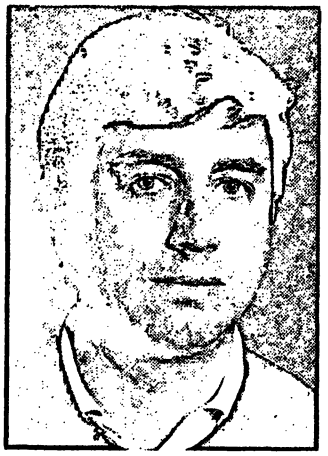
Routine ultrasound examination is performed on every obstetrical patient entering our department in the first half of pregnancy. These are patients from the antenatal clinics, referrals from outside hospitals and especially patients with an increased risk of genetic disorders.

The major goal of this examination is: 1. determination of gestational age and 2. early detection of abnormalities of pregnancy and fetal malformations.

Four of the five patients reported on here underwent a selective screening program to detect fetal abnormality by prenatal amniocentesis and one patient underwent routine ultrasound examination.

All ultrasound examinations were carried out alternatively with four different ultrasound instru-

Curriculum vitae



WERNER SCHMIDT, *born in 1944, received his Dr. med. from the University of Heidelberg in 1972, after studies in Frankfurt and Heidelberg. He specialized as an immunbiologist at the institute of immunology in Heidelberg (Head: Prof. Dr. K. O. ROTHER) from 1972–1974 with support of the Deutsche Forschungsgemeinschaft. Since November 1974 he is working in the Department of Obstetrics and Gynecology, University of Heidelberg, obtaining his specialist's qualification in Obstetrics/Gynecology in 1980 and the venia legendi in 1982. Main fields of research are: Perinatal medicine, ultrasound monitoring and immunology.*

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Tab. I. Comparison of our results with earliest diagnoses of severe fetal malformation syndromes reported in the literature.

Congenital disease	Author	Weeks	Own observation Weeks*
POTTER syndrome	HANSMANN, 1979 [14]	19	13
	KAFFE, 1977 [18]	21	
Anencephalic fetus	HANSMANN, 1979 [14]	13	13
	HOBBINS, 1979 [16]	15	
MECKEL-GRUBER syndrome (Encephalocele + polydactyly + polycystic kidneys)	FISHER, 1980 [12]	19	16
Exomphalos	HOFFBAUER, 1980 [17]	13	
	CAMPBELL, 1978 [10]	18	12
	THOULON, 1979 [30]	19	
Conjoined twins	MORGAN, 1978 [24]	23	11
	HANSMANN, 1979 [15]	27	

* (Completed weeks from last menstrual period)

ments: Combison 100 or Combison 200 compoundscan (2.5 MHz Kretz), M2130 (3.0 MHz ADR) and Superscan 50 (2.8 MHz Roche-Bioelectronics).

2.2 Case reports

2.2.1 Case 1, U. S.:

39 years old gravida II, para I was referred to the ultrasound unit with a menstrual age of 13 + 2 weeks. Because of advanced maternal age, prenatal amniocentesis was planned to exclude chromosomal anomaly. Prenatal amniocentesis was not carried out because of the ultrasonographically established diagnosis.

2.2.1.1 Ultrasonographic findings

Severe oligohydramnios was noticed already in the 14th week of pregnancy. Crown-rump length (67 mm) corresponded to the calculated gestational age. Fetal motor activity was recorded as infrequent (less than three spontaneous body movements/10 min). A fetal POTTER syndrome was suspected. Two additional examinations in the 15th and 17th week confirmed the diagnosis. After furosemide (Lasix®, 60 mg iv) application to the mother, nor filling of fetal bladder (within 60 minutes) neither fetal kidneys could be demonstrated. With consent of the parents, the pregnancy was terminated in the 19th week because of suspected POTTER syndrome (see Figs. 1a and 1b).

2.2.1.2 Pathoanatomical diagnosis: Bilateral renal agenesis, POTTER syndrome (PD Dr. H. REHDER, Lübeck).

2.2.2 Case 2, Ch. W.:

37 years old para 0, gravida I. The patient was referred to the University Hospital for prenatal amniocentesis because of advanced maternal age at 13 + 2 weeks gestational age.

2.2.2.1 Ultrasonographical findings

At her first ultrasound examination, an anencephalic fetus was diagnosed. Besides this, hydramnios was noticed (see Figs. 2a and 2b). The pregnancy was terminated in the 16th week.

2.2.2.2 Pathoanatomical diagnosis: Anencephalic fetus, 16th week of pregnancy.

2.2.3 Case 3, M. T.:

26 years old para I, gravida III. The first pregnancy was terminated in the 10th week in 1976. The second pregnancy (1979) ended with a stillbirth.

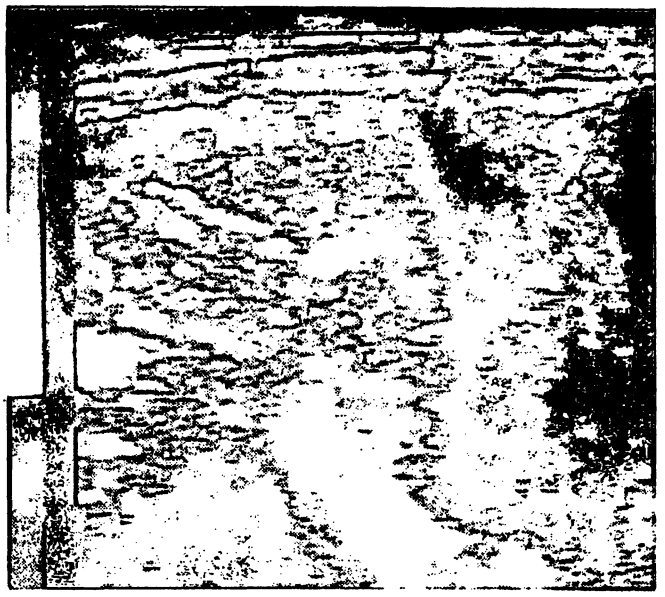

Fig. 1a. Fetus in longitudinal position 13 weeks of pregnancy. No amniotic fluid is to be seen. (Superscan 50, 2.8 MHz).

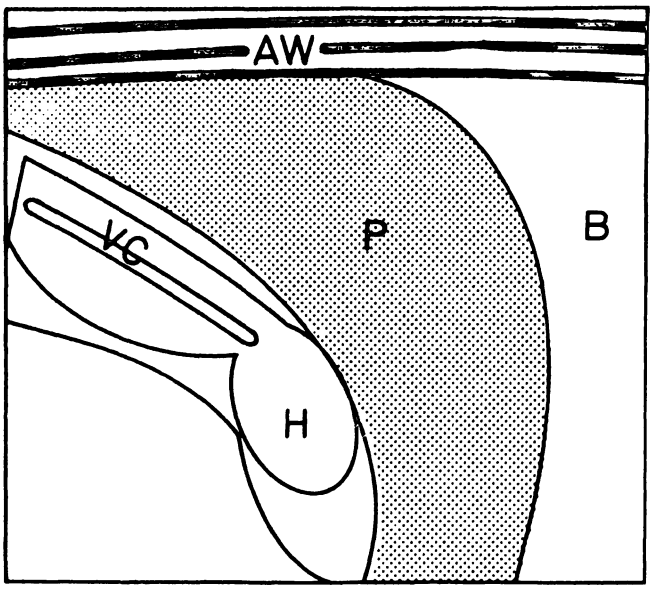

Fig. 1b. H = head, VC = vertebral column, P = placenta, AW = abdominal wall, B = bladder.

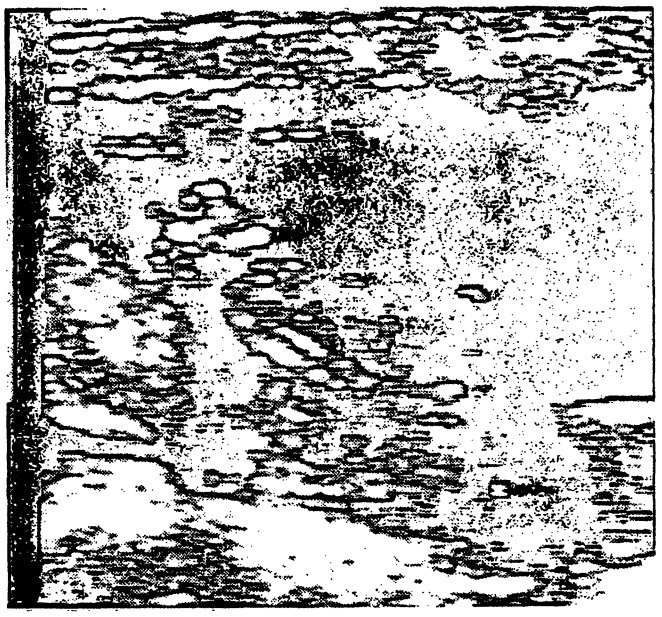

Fig. 2a. Anencephalic fetus 13 weeks of pregnancy. Massive hydramnios surrounds the fetus. (Superscan 50, 2.8 MHz).

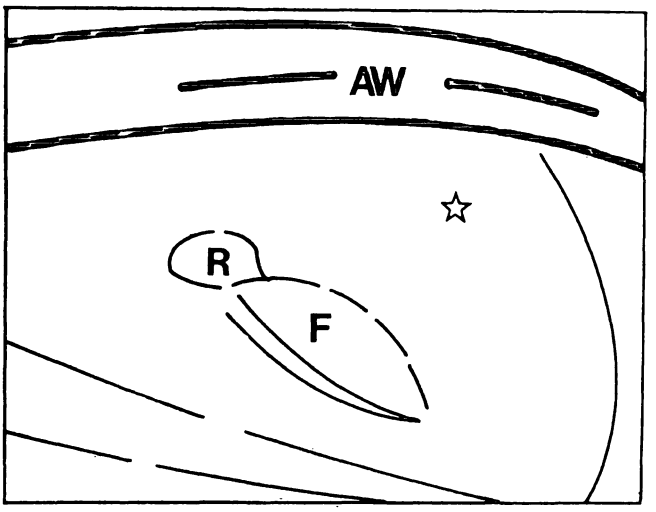

Fig. 2b. AW = abdominal wall, ☆ = hydramnios, F = fetal body, R = abnormal head.

The fetus had multiple malformations (hydrocephalus internus, hexadactyly, cyst of the liver, polycystic kidneys). A trisomy 13 was suggested in this case. Prenatal amniocentesis was recommended to the patient for the next pregnancy.

2.2.3.1 Ultrasonographical findings

At the first visit in the 15th week of pregnancy (14 + 5 weeks), a severe oligohydramnios with diminished fetal motor activity was observed and a fetal malformation was suspected. At the second visit (16 + 5 weeks), the oligohydramnios had increased and the suspected diagnosis of fetal POTTER syndrome was validated. The abdomen of the fetus was enlarged in comparison to the head (biparietal diameter 36 mm, thoracic transverse diameter 52 mm). In the ventral part of the fetal abdomen, a rounded cystic tumor could be demonstrated (diameter 20 mm) (see Figs. 3a and

3b). After furosemide application (Lasix®) to the mother, no filling of the fetal bladder could be demonstrated. Careful ultrasonographic examination with storage on videotape (U-matic, Sony) showed an osseous defect at the level of the occiput (4 mm diameter). The vertebral column, however, was normal in longitudinal and transverse scan investigation. An echodense structure lying outside the occiput could be identified and thought to be a possible encephalocele (see Figs. 4a and 4b). At amniocentesis, dark green amniotic fluid was aspirated. Alpha-fetoprotein was elevated (maternal serum 273 µg/ml; amniotic fluid 170000 µg/m), cytogenetic investigation revealed a normal female karyotype. Acetycholinesterase activity was also pathologically elevated (27 mU/ml). Taking these data together with the ultrasound findings, MECKEL-GRUBER syndrome was suspected. The pregnancy was terminated for fetal reasons in the 19th week.

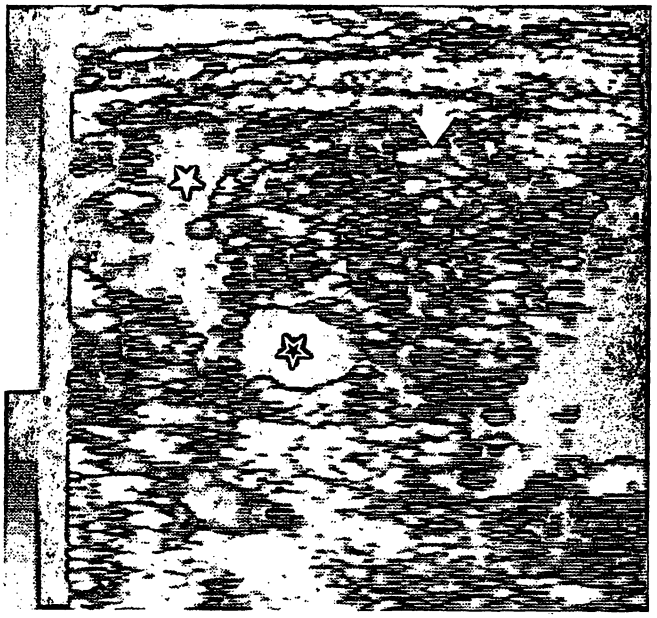

Fig. 3a. Fetal abdomen with cystic tumor in the ventral part ☆. (Superscan 50, 2.8 MHz).

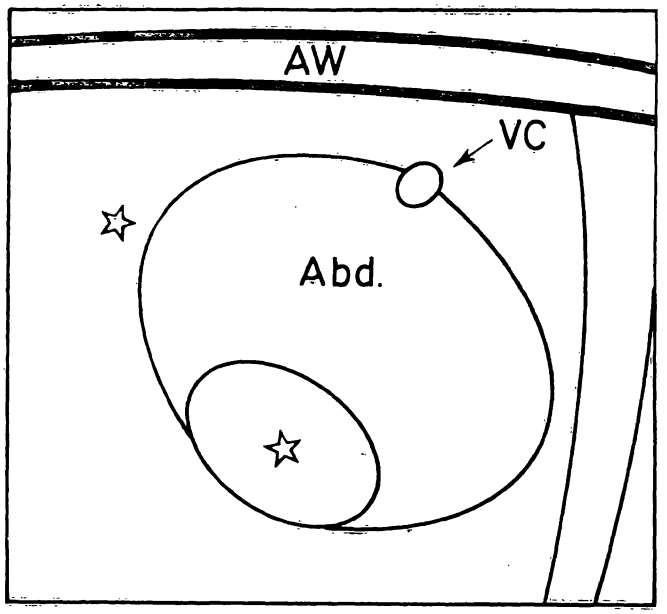

Fig. 3b. AW = abdominal wall, Abd = fetal adimen, ↓VC = vertebral column, ☆ = oligohydramnios.

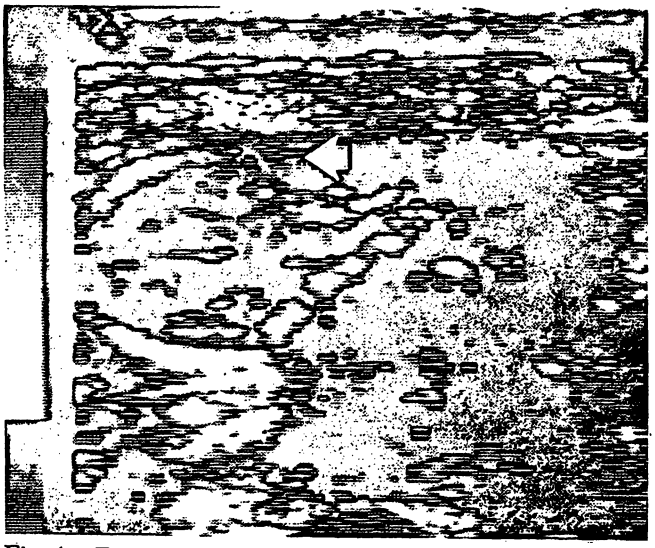

Fig. 4a. Fetal head with encephalocele ←. (Superscan 50, 2.8 MHz).

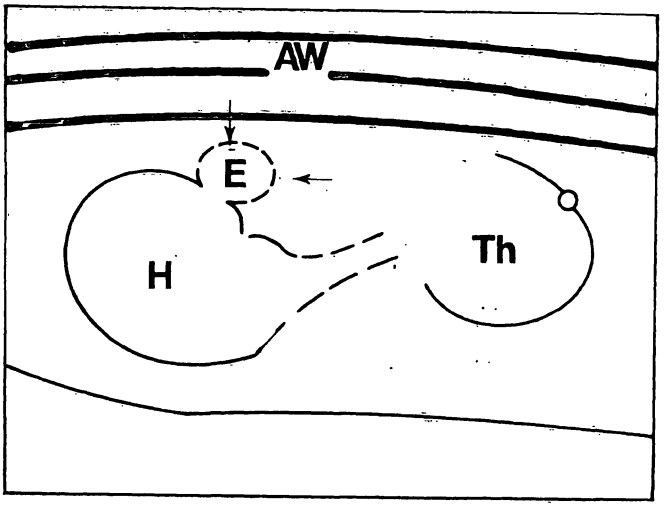

Fig. 4b. AW = abdominal wall, H = fetal head, ← = encephalocele, Th = fetal thorax.

2.2.3.2 Pathoanatomical diagnosis: Fetal MECKEL-GRUBER syndrome (encephalocele, polycystic kidney and polydactyly) (PD Dr. H. REHDER, Lübeck).

2.2.4 Case 4, B. D.:

42 year old patient, para I, gravida II. The patient was referred for ultrasonographic examination and amniocentesis because of advanced maternal age.

2.2.4.1 Ultrasonographical findings

At her first visit in the 13th week (12 + 4 weeks), fetal biometry corresponded to the gestational age (crown-rump length 67 mm, biparietal diameter 23 mm). However, outside the fetal abdomen at the umbilicus, an echodense-structured tumor could be detected in the longitudinal as well as in transverse scan examination (see Figs. 5a and 5b, 6a and 6b). Fetal exomphalos was assumed. In the 15th week, the suspicion was validated by repeti-

Fig. 5a. Fetus longitudinal position with large ↓ omphalocele. (Superscan 50, 2.8 MHz).

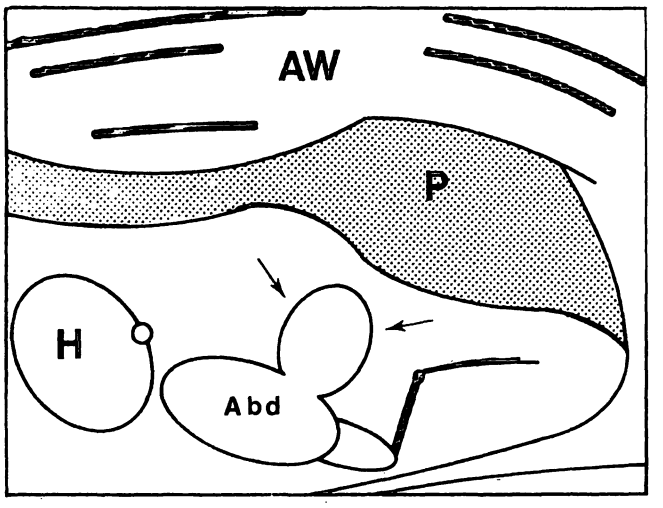

Fig. 5b. AW = abdominal wall, H = fetal head, Abd = fetal abdomen, ↓ = omphalocele.

Fig. 6a. Fetus transverse scan. Intestinum outside the fetal abdomen ↓ (omphalocele). (Superscan 50, 2.8 MHz).

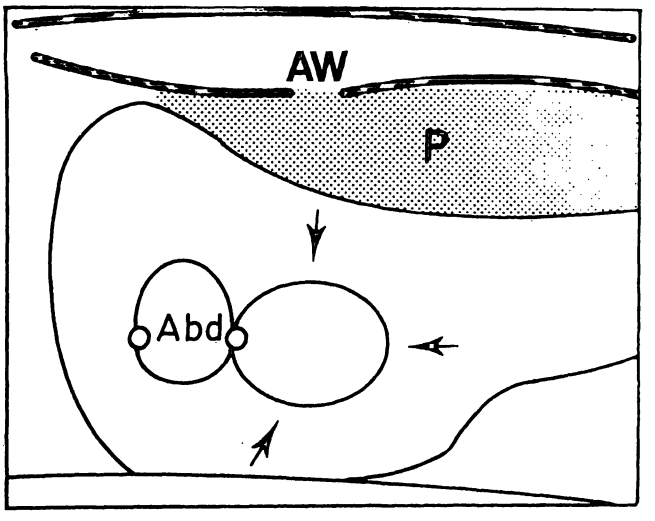

Fig. 6b. AW = abdominal wall, P = placenta, ABD 3 = fetal abdomen, ↓ = omphalocele.

tion of ultrasound examination. Alpha-fetoprotein values (25000 µg/ml) and acetylcholinesterase activity (6 mU/ml) were found to be elevated. The pregnancy was terminated in the 17th week. Cytogenetic examination (three weeks after termination of the pregnancy) revealed a chromosomal anomaly: trisomy 18.

2.2.4.2 Pathoanatomical diagnosis: Fetal omphalocele with further characteristic symptoms of trisomy 18 (PD Dr. H. REHDER, Lübeck).

2.2.5 Case 5, U. Sch.:

23 year old patient, I para, II gravida. First visit to the outpatient department in the 12th week of pregnancy (11 + 6 weeks). Ultrasonographic routine examination was performed at the same time.

2.2.5.1 Ultrasonographic findings

Ultrasonographic examination revealed a monoamniotic twin pregnancy (biparietal diameter 19 mm of each twin and a fetal crown-rump length of 56 mm). The placenta was found at the anterior wall of the uterus. However, real-time scan observation showed that each fetus was moving at the same time as the other. Inspection of the fetal abdominal region provided the explanation for this: both fetuses were fused together at the ventral body region. With time-motion display technique, two differently beating hearts could be identified: (fetus 1: 170 beats/min, fetus 2: 180 beats/min). The contours of both fetal abdomens showed no separation in transverse scan examination (see Fig. 7a and 7b). The diagnosis of conjoined twins was established and the pregnancy terminated with the consent of the parents.

2.2.5.2 Pathoanatomical diagnosis: "Siamese twins" with one giant liver for both fetuses.

3 Discussion

The incidences of severe fetal congenital malformations presented in this investigation vary between 1:1,000 (anencephaly), 3:10,000 (POTTER syndrome), 1:6,000 (exomphalos), 1:50,000 (MECKEL-GRUBER syndrome) and 1:250,00 (conjoined twins) live births [2].

Ultrasonographically detectable malformations are most often neural tube defects. CAMPBELL et al. [6] and CAMPBELL [9] described the ultrasono-

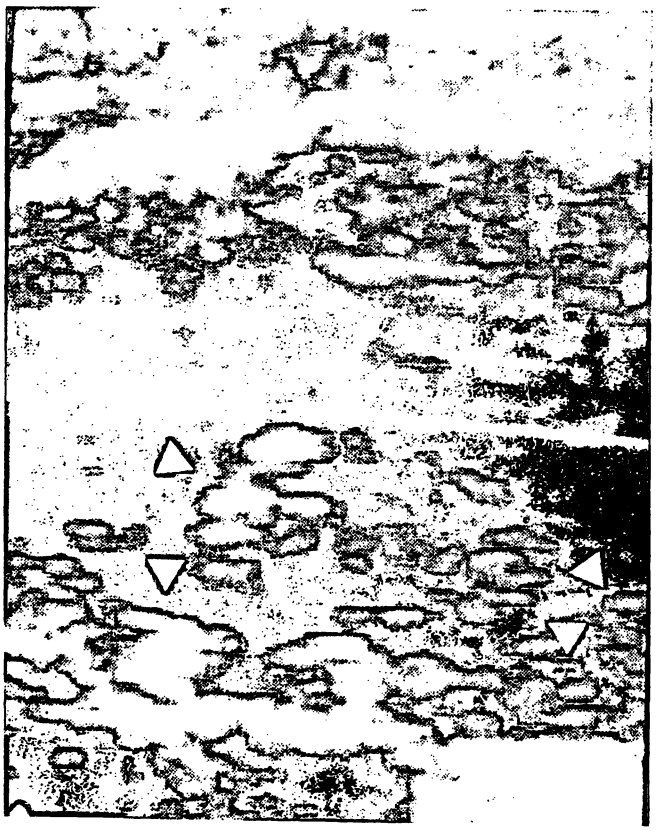

Fig. 7a. Conjoined twins 12th week of pregnancy. En face position. Thoracoabdominopagus. The contours of both fetuses are fused.

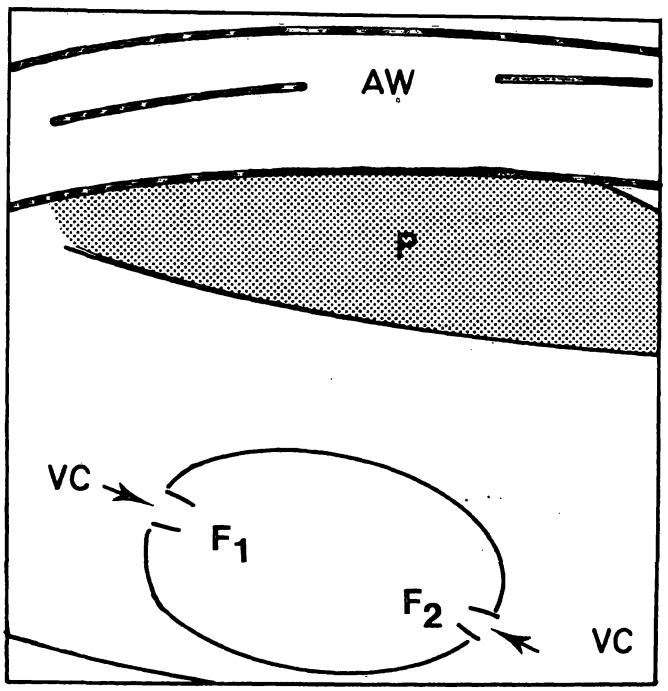

Fig. 7b. AW = abdominal wall, P = placenta, F_1 = fetus 1, F_2 = fetus 2, $\triangle\,\triangledown$ = vertebral columns.

graphic symptoms of malformations of the neural tube. Early diagnosis (13 weeks) of an anencephalic fetus was reported by HANSMANN [14].

Detection of fetal "POTTER syndrome" by the use of ultrasound examination was introduced by GARRETT et al. [13]. Many subsequent reports deal with this mostly nonviable fetal congenital anomaly [14, 27]. Original POTTER syndrome, presented in this article, was diagnosed on the basis of the most important symptom in fetal urinary tract anomalies, namely anhydramnios. The anhydramnios was caused by total agenesis of both fetal kidneys. CAMPBELL et al. [7, 11] have been able to show that the filled bladder could be demonstrated within 60 min after furosemide application to the mother in cases with normal urinary tract. According to KURJAK [22] the use of the furosemide test is of no help to prove the non-filling process of the fetal bladder, because tubular reabsorption is not established before the 20th week of pregnancy. Alternatively the inability to fill the bladder can also be evaluated by repeated ultrasound examinations with longer observation periods (60–120 min.). At best, however, malformations of the urinary tract are detected in advanced stages of gestation. If amniotic fluid volume and visualization of fetal kidneys is taken into consideration with every ultrasound examination, fetal POTTER syndrome could be detected before the end of the 20th week in nearly all cases [27].

Antenatal diagnosis of MECKEL-GRUBER syndrome (encephalocele, polycystic kidneys and polydactyly) by means of ultrasonography was described by AULA et al. [1] in the third trimester of pregnancy. This rare malformation syndrome consists of the triad: Encephalocele, polycystic kidney disease and polydactyly. In 1978, MISKIN et al. [23] presented a case with occipital encephalocele diagnosed by ultrasound in the second half of pregnancy. The diagnosis of occipital encephalocele presented here could be established by storage of the whole ultrasound procedure on videotape and thorough and repeated inspection of the fetal head and vertebral column at intervals thereafter.

Determination of alpha-fetoprotein values from amniotic fluid or maternal serum is the classical method for biochemical detection of neural-tube defects [4, 8]. Acetylcholinesterase activity is also regarded as helpful in detecting anomalies of the neural tube with certainty [29].

In our opinion, polydactyly cannot be visualized reliably by ultrasound. Fetoscopy might give better results although performance of fetoscopy is also influenced by the amount and the colour of amniotic fluid [28].

Early assessment of fetal exomphalos was reported by HOFFBAUER [17] and CAMPBELL et al. [10]. The diagnosis was made in one case already in the 14th week and in three cases between the 18th and 20th week of pregnancy. In our case, the suspicion of fetal exomphalos as early as the 13th week resulted from characteristic sonographic signs. The prolapsed intestine and the liver were demonstrable by transverse as well as in longitudinal section of the fetal body. Alpha-fetoprotein values are often elevated in cases with fetal omphalocele [5]. Very often defects of the anterior wall of the fetus are associated with other congenital anomalies and even chromosomal anomalies [25]. Acetylcholinesterase activity which is regarded as specific for neural-tube defects, was also prepathological in our case with exomphalos.

HANSMANN et al. [15] have described the prepartal diagnosis of conjoined twins in the third trimester of pregnancy. The authors stated that the additional use of fetal amniography gave no improvement in the antenatal examination procedure. In the case presented, the antenatal diagnosis of conjoined twins was performed by routine ultrasound examination in the 12th week of pregnancy [26].

In neither of the five cases was additional amniography necessary to verify the ultrasonographically suspected diagnosis. In fact, four of the five patients presented were part of a selective screening program for congenital malformations on the basis of advanced maternal age and/or history and in three of them the diagnosis would have been established also by amniocentesis. However, **the high and still increasing reliability of ultrasound as a means of diagnosing congenital malformations associated with structural fetal abnormalities renders routine systemic screening by this non-invasive method an attractive possibility at this stage of pregnancy.**

Summary

The significance of ultrasound examinations in early stages of pregnancy is illustrated by the detection of four severe congenital malformations within the first trimester and one malformation syndrome within the first part of the second trimester of pregnancy. We report on the diagnosis of a fetal POTTER syndrome (13 weeks), an anencephalic fetus (13 weeks), MECKEL-GRUBER syndrome (16 weeks), fetal exomphalos (12 weeks) and finally "Siamese twins" (11 weeks). Characteristic ultrasonographic findings are presented and described in detail.

The incidence of these severe fetal abnormalities vary between 1:1000 (anencephaly), 1:6000 (exomphalos), 3:10000 (POTTER-Syndrome), 1:50000 (MECKEL-GRUBER Syndrome) and 1:250000 (conjoined twins) live births. The sonographical diagnosis of all these malformation syndromes could be established by thorough and repeated inspection of the fetal head and fetal body with longitudinal and transversal scans.
It is concluded, that the high and still increasing reliability of ultrasound examination as a means of diagnosing congenital structural anomalies renders routine systemic ultrasound screening an attractive possibility already at this "early" stage of pregnancy.

Keywords: Congenital malformations, monitoring, pregnancy, ultrasound examination.

Zusammenfassung

Die „frühzeitige" Diagnose schwerer fetaler Mißbildungs-Syndrome durch Ultraschall
Die Bedeutung der „frühen" Ultraschalluntersuchung wird durch die Erkennung von vier schweren fetalen Mißbildungssyndromen innerhalb des ersten Schwangerschaftstrimesters und eines kongenitalen Mißbildungssyndroms zu Beginn des zweiten Trimenons unterstrichen. Wir berichten über die Diagnose eines originären POTTER-Syndroms (13 Schwangerschaftswochen), über die Diagnose eines Anencephalus (13 Schwangerschaftswochen), eines MECKEL-GRUBER-Syndroms (16 Schwangerschaftswochen), einer fetalen Omphalocele (12 Schwangerschaftswochen) und zuletzt über die sonographische Feststellung von ‚siamesischen Zwillingen' (11 Schwangerschaftswochen). Die charakteristischen ultrasonographischen Befunde werden vorgestellt und ausführlich erörtert.

Die Häufigkeit dieser schweren fetalen Mißbildungen variiert zwischen 1:1000 (Anencephalus), 1:6000 (Omphalocele), 3:10000 (POTTER-Syndrom), 1:50000 (MECKEL-GRUBER Syndrom) und 1:250000 (siamesische Zwillinge) Lebendgeburten. Die ultrasonographische Diagnose der vorgestellten Mißbildungssyndrome konnte durch gründliche und wiederholte Inspektionen des fetalen Körpers (Kopf- und Rumpfregion einschließlich der Extremitäten) mit Longitudinal und Transversalschnitten erstellt werden.
Aufgrund der zunehmenden Zuverlässigkeit ultrasonographischer Untersuchungsergebnisse bei der Diagnose schwerer kongenitaler Mißbildungssyndrome stellt ein sog. „Ultraschall-Screening" auch zu diesem „frühen" Zeitpunkt der Schwangerschaft eine bedeutende Untersuchungsmethode dar.

Schlüsselwörter: Kongenitale Mißbildungen, Schwangerschaftsüberwachung, Ultraschalluntersuchung.

Résumé

Le diagnostic précoce des syndromes de malformations fétales graves au moyen de l'ultra-son
Le dépistage de quatre malformations fétales graves lors du premier trimestre de la grossesse et d'une malformation congénitale au début du second trimestre soulignent l'importance de l'ultra-son faite tout au début de la grossesse. Nous aimerions parler du diagnostic d'un syndrome de POTTER typique (13 semaines de grossesse), du diagnostic d'un cas hydrocéphale (13 semaines de grossesse), d'un syndrome de MECKEL-GRUBER (16 semaines de grossesse), d'un omphalocele (?) fétal (12 semaines de grossesse), et enfin de la découverte de l'ultra-son de frères sianois (11 semaines de grossesse). Les résultats charactéristiques de l'ultra-son seront présentés et discutés en détail.

Le grad nombre de ces malformations fétales graves varient entre 1:1000 (le syndrome hydrocéphale), 1:6000 (le syndrome d'omphalocele (?)), 3:10000 (le syndrome de POTTER), 1:50000 (le syndrome de MECKEL-GRUBER), et 1:250000 (le syndrome de frères siamois) enfants qui sont venus au monde vivants. On pouvait établir le diagnostic par l'ultra-son de ces malformations présentées par suite de plusieurs examens détaillés du corps fétal (la tête, le tronc et les extrémités) en mettant l'appareil ultra-son longitudinalement et transversalement. A cause de la sûreté des résultats de l'examen par l'ultra-son pour le diagnostic des malformations congénitales graves, qui s'intensifie de plus en plus, un soi-disant "ultra-son-screening" représente une méthode d'examen importante déjà tout au début de la grossesse.

Mots-clés: Examen à l'ûltra-son, malformations congénitales, surveillance de la grossesse.

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